UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/099,924	03/14/2002	Daniel Albert Wettstein	1909.03	2745

26698 7590 09/01/2005

MYRIAD GENETICS INC.
INTELLECUTAL PROPERTY DEPARTMENT
320 WAKARA WAY
SALT LAKE CITY, UT 84108

EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 09/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/099,924	WETTSTEIN ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04/04 & 05/05/05*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-26 and 40-50* is/are pending in the application.

4a) Of the above claim(s) *11-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments and Arguments

1. Claims 11-26 and 40-50 are pending.

Claims 40-50 have been added.

Claims 40-42 have been amended.

Claims 1-10 and 27-39 have been cancelled.

Claims 11-26, drawn to non-elected inventions are withdrawn from examination.

Claims 40-50, to the extent that the second protein is HDLC1 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections

Oath/Declaration

3. Applicants have submitted a new declaration on April 4, 2004 citing all the priority documents from which they request benefit. The former declaration filed May 28, 2002 did not include U.S. Provisional Application number 60/307,233 filed on July 23, 2001.

Claim Objections

4. Claims 1, 2, 4, 5 and 7 are no longer objected to because they have been cancelled.

Specification

5. The first line of the specification has been amended to include all priority applications, see the amendment submitted April 4, 2005.

6. The disclosure is no longer objected to because it no longer contains an embedded hyperlink and/or other form of browser-executable code, see page 17, line 29; page 18, line 5.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

7. The rejection of claims 1-5, 7 and 39 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement has been withdrawn in light of the cancellation of the claims.

8. The rejection of claims 1-5, 7 and 39 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn in light of Applicants' cancellation of the said claims.

9. The rejection of claims 1-5, 7 and 39 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

which applicant regards as the invention is withdrawn because the claims have been cancelled.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

10. Claims 40-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **THIS IS A NEW MATTER REJECTION.**

Amended and new claims 40(b), (ii); 43; 45(b),(c),(ii),(iii); 49; and 50. Specifically, claim 40 includes the recitations, " (b) a first polypeptide having...at least 80% identical to that..." and "(ii) a second polypeptide having...at least 80% identical to that ...". Claim 43 cites "...fragments of survivin comprises amino acid residues...47 to 99 of survivin." Claim 45 includes the recitations:

"(b) a survivin fragment containing a contiguous span of 10 amino acid residues..." ;

"(c) a first polypeptide having an amino acid sequence at least 90% identical to that..."'

"(ii) an HDLC1 fragment comprising a contiguous span of 10 amino acid residues..."; and

"(iii) a second polypeptide having an amino acid sequence at least 90% identical to that...". And claims 49 and 50 claims cite at least 80% and 90% identical to that of particular fragments defined by specific amino acid residues, respectively.

Applicants have not pointedly expressed by page and line number where support for these recitations and citations can be found. It is clear that Applicants have support for specific binding regions of survivin and interacting partner, HDLC1 fragments, see Table 1 on page 21. The specification seems to be remiss of amino acid residues 47 to 99 of survivin interact with HDLC1, fragment thereof, a polypeptide 80% or 90% identical to HDLC1. Likewise, it is unclear where in the specification Applicants have contemplated only 80%, 90% or a contiguous span of 10 amino acids of a first polypeptide, survivin interacting with at least 80%, 90% or a contiguous span of 10 amino acids of a second polypeptide. Applicants have not noted in the Remarks submitted April 4, 2005 and May 5, 2005 where support for these specific contemplations can be found in the disclosure. Accordingly, these claims contain new matter. The claims should be cancelled, text deleted from the claims or the support should be specifically pointed out by page and line numbers to obviate the instant rejection.

11. Claims 40-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In anticipation of the instant rejection Applicants assert that the same rejection would be applied to claims 40-46. That is not the case, dependent claims are also rejected as well as claims containing the less than 100% sequence identity language. In support of their claim language Applicants refer to the Training Materials. Applicants state that "...-survivin and HDLC1-specifically interact with each other." and specific fragments of the said interacting proteins are indicated in the specification, see Remarks, section IV beginning on page 12, submitted April 4, 2005. These points of view and arguments have been carefully considered, but found unpersuasive.

Applicants broadly claim an isolated protein complex having a first protein, which is survivin, fragment thereof, 10 contiguous amino acid residues or polypeptide having at least 80%-90% sequence identity to survivin or survivin fragment which interacts with a second protein which is human cytoplasmic dynein light chain 1 (HDLC1) or fragment thereof, 10 contiguous amino acid residues or polypeptide having at least 80%-90% sequence identity to survivin or survivin fragment. The written description in this instant case only sets forth first protein, survivin which is 142 amino acids long (GenBank Accession number U75285) and second protein, HDLC1 which is an 89 amino acid protein (GenBank Accession number U32944), as well as the specific fragments cited in Table 1 on page 21. Therefore the written description is not commensurate in scope with the claims drawn to an isolated protein complex having less than 100% sequence identity to survivin or less than 100% sequence identity to specific fragments of survivin

listed in Table 1 and less than 100% sequence identity to HDLC1 or less than 100% sequence identity to specific fragments of HDLC1 listed in Table 1. Furthermore, Applicants are only in possession of an isolated protein complex consisting of isolated protein complexes of survivin (amino terminus residues 3-99), (carboxy terminus residues 89-142) and core binding site residues 89-99 of survivin which specifically interact with HDLC1, see the specification, Table 1; page 23, lines 6-31; and page 24, lines 21-24. Applicants are not in possession of essentially any and all homologues, derivatives or fragments of the first and second proteins within an isolated protein complex or fusion protein. The homologues and derivatives more than likely comprise undefined amino acids that would not resemble the art known proteins, survivin and HDLC1 as defined by their corresponding GenBank Accession numbers.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Applicants are not required to disclose every species encompassed by a genus. For example as indicated in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the description of a genus is achieved by the recitation of a

representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Applicant is only in possession of the fragment species of survivin and HDLC1 listed in Table 1, see page 21. Applicants have characterized the 3 sets of bait/binding protein regions of survivin and its interacting partner, HDLC1 prey/interactor protein regions. Applicants are not in possession of unidentified and uncharacterized homologues, derivatives and fragments thereof of survivin and its interacting partner, HDLC1. Applicants are not permitted to claim all possible peptide combinations comprised within the claimed isolated protein complex or fusion proteins that are encompassed by the claims, hence not entitled to the wide breadth of the claims at issue. As Applicants' claims are written they encompass variants, as well as sequences yet to be discovered. There is no description of the sites at which variability may be tolerated. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. One skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicants' attention is directed to the Official Gazette, Volume 1242 published January 30, 2001. On page 1242 OG 174, column 1, section 2 "[t]he written description requirement for a claimed genus may be satisfied through sufficient description of a

representative number of species by actual reduction to practice...". Applicants have not provided evidence substantiating they are in possession of the entire genus reading on polypeptides 80% or 90% sequence identical to survivin or HDLC1 and moreover fragments sharing 80% or 90% sequence identity to fragments of survivin comprising 97 and 53 residues long. This section of the OG clearly sets forth "where there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus." Information regarding how to make a variant or an assay for detecting the activity of a variant is not a showing of possession of the entire genus claimed. It is clear that the species identified in the specification attributing to the interaction between survivin and HDLC1 consists of critical structure as indicated in applicants' specification, see page 23, lines 25-31.

There continues to be insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph.

12. Claims 40-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In anticipation of the instant rejection Applicants Remarks directed to the instant rejection provide evidence, Exhibit A corroborating the Examiner's position, the amino acid sequence of a polypeptide determines its structural and functional properties. Applicants assert the first action on the merits office action mailed December 02, 2004 misplaces the focus on predictability at the individual amino acid level. Additionally, Applicants note the Training Materials in support of the traversal of the instant application. The Exhibit, as well as Applicants' arguments and points of view have been carefully considered but found unpersuasive.

Applicants are reminded while one of ordinary skill in the art can theoretically produce all of these proteins with art known techniques such as site-directed mutagenesis it would still be burdensome to one of ordinary skill in the art to produce all of these different combinations and thereafter determine their activity. Applicants broadly claim an isolated protein complex having a first protein, which is survivin, fragment thereof, 10 contiguous amino acid residues or polypeptide having at least 80%-90% sequence identity to survivin or survivin fragment which interacts with a second protein which is human cytoplasmic dynein light chain 1 (HDLC1) or fragment thereof, 10 contiguous amino acid residues or polypeptide having at least 80%-90% sequence identity to survivin or survivin fragment. The wild type proteins are depicted in the GenBank Accession numbers referenced on page 21. The claims continue to encompass undefined and uncharacterized protein fragments, fusion proteins, peptides, homologues and derivatives.

Applicants state "...[their] disclosure will predictably be able, by routine deletions, insertions, and/or substitutions techniques, to make the variants called for in the new [c]laims...", see bridging sentence of pages 15 and 16 of the Remarks. While one of ordinary skill in the art can theoretically produce all of these proteins with art known techniques it is burdensome to one of ordinary skill in the art to make and use these different combinations and thereafter determine their activity. Applicants' disclosure has not set forth any criteria as guidance to know which residues should be modified or deleted. Granted that is undue experimentation given that this would require a level of ingenuity beyond what is expected from on of ordinary skill in the field. To further substantiate The Examiner's position Applicants are requested to review sequence 2 of U.S. Patent 6,168,926 (issued January 2, 2001). Sequence 2 is 100% sequence identical to HDLC1, however sequence 2 is not recognized as a HDLC1, but a rat protein inhibitor of nitric oxide, see sequence listing, columns 15-18. It is reasonable to those in the art high sequence identity cannot be used as the sole standard for the ability to use. And U.S. Patent number 6,800,737 (issued March 9, 2004) presents sequence 6,392, which is at least 82.5% sequence identical to survivin, however it is identified as an expressed sequence tag not completely identified or characterized. It is clear from Applicants' claims they embody survivin and HDLC1 variants that address and read on polypeptides other than survivin and HDLC1.

There is no guidance of record setting forth the strategy of obtaining the broadly claimed isolated protein complex comprising survivin homologues, derivatives and fragments interacting with HDLC1 homologues, derivatives and fragments. The

peptide art is unpredictable with regard to determine what peptides resulting form deletions, additions, mutations or analogues would be biologically active. Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acid or acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved and detailed knowledge of the ways in which the protein's structure relates to its function. The specification provides essentially no guidance as to which of the infinite possible choices is likely to be successful in making the complex and using the complex in the manner suggested by the specification.

From the analysis established above and of record it is clear that the predictability of changes to an amino acid sequence is practically nil as far as biological activities are concerned. The specification fails to provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed polypeptides in a manner reasonably correlated with the broad scope of the claims. Without such guidance, the changes which can be made in the protein structure and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016 and *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 6:30 am to 5:30 pm with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alana M. Harris, Ph.D.
25 August 2005
ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER